

Obstacles in the Path? Medicare's National Coverage Determination on Next-Generation Sequencing Has Significant Implications for Precision Medicine

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A controversial new [Medicare national coverage determination](#) (“Medicare NCD”) for certain next-generation sequencing (“NGS”) tests published by the Centers for Medicare & Medicaid Services (“CMS”) on March 16, 2018, could have a significant impact on clinical laboratories developing and offering NGS-based testing for cancer diagnosis and treatment. Under the new Medicare NCD, only “companion” in vitro diagnostic (“IVD”) devices can be Medicare-covered tests nationwide—and solely for Medicare patients with advanced cancer. The Medicare NCD would give Medicare administrative contractors (“MACs”) discretion to cover other NGS-based tests not meeting these criteria (although whether and how MACs will choose to do so remains uncertain). The Medicare NCD also may deter private commercial payors from covering these tests, which could limit patient access to these tests.

A “companion diagnostic” is an IVD device that “provides information that is essential for the safe and effective use of a corresponding therapeutic product.” As the U.S. Food and Drug Administration (“FDA”) considers companion diagnostics essential, the use of an IVD companion diagnostic must be stipulated in the instructions for use of both the therapeutic product and the approved IVD device.

Currently, there are just four FDA-approved tests that meet the new Medicare NCD criteria. Many cancer diagnostic tests, including those that use NGS technology, are performed by clinical laboratories as laboratory developed tests (“LDTs”)—which do not require FDA review. Even if an NGS test does receive FDA marketing authorization, the NGS test will not be covered nationally under the Medicare NCD unless it is designated as a “companion” diagnostic.

What Is NGS?

NGS is a method for rapidly sequencing large segments of the human genome. NGS technology can substantially increase the efficiency and accuracy of genetic sequencing and lower its cost. Consequently, NGS has been adopted rapidly by both genetic

researchers and by some clinical laboratories, and NGS has supplanted older technologies, such as Sanger sequencing, as the preferred method for large-scale gene sequencing.

Current uses of NGS testing in oncology include the detection of both inherited and sporadic mutations in individuals diagnosed with cancer. This information can help guide treatment decisions, including the selection of therapeutic agents. NGS testing also is used in cancer predisposition testing to identify certain heritable mutations that increase cancer risk. An ongoing challenge arising from the rapid clinical integration of NGS testing is the need for evidence correlating mutations with patient symptoms and prognosis (clinical validity) as well as evidence demonstrating that testing patients leads to better health outcomes (clinical utility). A number of government agencies and professional organizations have been focused on developing standards for NGS test development and validation and to create mechanisms for systematic data collection.

Medicare Coverage Requirements

The Medicare statute provides that services associated with technologies like NGS testing can be Medicare-covered only if “reasonable and necessary” for the diagnosis or treatment of an illness or injury. Coverage and reimbursement also may be available on a temporary basis through the “Coverage with Evidence Development” (“CED”) policy if CMS determines that the item or service can be reasonable and necessary, but that further clinical studies or additional data collection are still needed to make a final determination. CMS uses a defined process for reaching national coverage determinations.

The New Medicare NCD

The NGS Medicare coverage determination review was requested by a developer of a comprehensive genomic profiling test. Although the test developer had not initially submitted the test for FDA review because the test is an LDT that the agency has generally not regulated, the developer ultimately obtained approval through FDA’s Breakthrough Devices program. The developer also sought parallel FDA and CMS review, under which both agencies review data simultaneously to streamline the approval and coverage decisions.

The NGS Medicare coverage determination review, finalized in the March 16, 2018, decision memo, applies to all NGS-based companion diagnostics, not just to the test that was the subject of parallel review. The new coverage decision operates largely within a framework in which different coverage rules apply depending on the route to market for a given NGS test. Nevertheless, the final Medicare NCD as adopted by CMS creates disincentives for LDTs, which historically have not been subject to FDA review.

The final Medicare NCD sets up two possible pathways to Medicare coverage with very different criteria and levels of certainty. Under both pathways, NGS testing must be ordered by a treating physician and performed in a CLIA-certified laboratory. Both pathways would exclude newly diagnosed cancer patients and those with earlier-stage

disease. The final Medicare NCD also jettisoned the option for CED for tests that were not FDA approved “companion” diagnostics.

NGS as an FDA-Cleared or -Approved Companion IVD

Under the first pathway, effective immediately Medicare coverage will be available for patients who have “recurrent, relapsed, refractory, metastatic, or advanced stages III or IV cancer,” who have not been tested previously with the same NGS test, and who have decided to undergo cancer treatment such as chemotherapy. The NGS test must be performed by a CLIA-certified laboratory and must be (i) an FDA-approved companion *in vitro* diagnostic, (ii) used in accordance with the FDA-approved indication for use, and (iii) reported to the treating physician using a report template to “specify treatment options.”

Potential Medicare Coverage for Other NGS Tests

Under the second pathway, coverage may be available for tests that are not FDA-approved companion diagnostics at the discretion of the local MACs that handle the Medicare fee-for-service claims filed by providers and suppliers. The Medicare NCD would limit a MAC’s coverage discretion to patients who have (i) “recurrent, relapsed, refractory, metastatic, or advanced stages III or IV cancer”; (ii) not been tested previously using the same NGS test for the same primary cancer; and (iii) elected to undergo further cancer treatment, such as chemotherapy.

Stakeholder Response

More than 300 comments were submitted to CMS in response to a draft local coverage determination (“LCD”) for NGS that was issued on November 30, 2017. While some commenters expressed support for aspects of the proposal, a majority raised significant concerns about the adverse impact of the limitations imposed by the proposed Medicare NCD on patient access to existing tests and to the development of new NGS-based tests. They warned that not all NGS-based tests are the same, and many criticized CMS’s fundamental approach of making a coverage decision based on the method used by a laboratory to perform testing rather than on the type of test performed using that method, which, they cautioned, could lead to the use of other less effective technologies to perform testing.

With respect to the CED pathway, many stakeholders expressed concern about the inability of clinical laboratories to meet the data collection requirements proposed by CMS; some proposed changes to the CED requirements to reduce the burden on individual clinical laboratories.

Stakeholders also were largely critical of CMS’s proposal to exclude all tests other than FDA-approved companion diagnostics from the first category, arguing that many established LCDs currently in place for scientifically valid and medically necessary NGS-based laboratory tests would be eliminated. A few stakeholders strongly supported the reliance on FDA approval, viewing FDA’s historically rigorous quality requirements

for manufacturers as necessary for coverage of NGS-based tests and the further integration of such tests into clinical practice.

Analysis

A new technology's FDA profile has long been a Medicare coverage consideration; however, this has not been the case with LDTs because FDA has historically exercised "enforcement discretion" with respect to such tests. While FDA has, at various times, considered comprehensive LDT regulation, in 2017 FDA decided to discontinue development of a proposed regulatory framework after concluding that more research and discussion with stakeholders was needed. Ironically, the Medicare NCD indirectly reopens the LDT debate by restricting Medicare national coverage to LDTs that have received FDA approval as companion diagnostics.

The Medicare NCD excludes several large categories of potential patients; no Medicare coverage would be available for NGS tests performed for patients with stage I or II cancers, and Medicare coverage is not available for tests performed for patients with an initial cancer diagnosis, even if chemotherapy is the preferred treatment option.

Also, the Medicare NCD abandoned a CED proposal in the November 30, 2017, draft LCD that would have permitted Medicare coverage for NGS tests that have not been approved or cleared by FDA, as long as the Medicare beneficiaries are enrolled in an NIH-NCI National Clinical Trial Network clinical trial where the NGS test is part of the trial protocol. In its review of the submitted comments, CMS explained that CED was unnecessary because there already are studies underway to evaluate the impact of NGS on health outcomes. Nevertheless, by foreclosing a CED option and potential Medicare reimbursement, developers, laboratories, and other stakeholders may face an additional barrier that may significantly delay or deter the development of new NGS assays.

The portion of the Medicare NCD that may create the most ambiguity involves tests subject to MAC discretionary coverage. The Medicare NCD does not identify the criteria that MACs should use to make a coverage decision for an individual NGS test. Without any further guidance, MACs have the option to (i) cover NGS tests on a case-by-case basis, (ii) apply the criteria in the *Medicare Program Integrity Manual* that apply to LCDs, or (iii) issue their own LCDs, which can range from fully positive to fully negative. The lack of criteria in the Medicare NCD could make it difficult to challenge a MAC's denial of coverage, since it would be more difficult to argue that a denial of coverage is either contrary to the available evidence or completely arbitrary.

Even when a MAC decides to cover an NGS test, laboratories should be careful to retain documentation that the test results were reported to the treating physician for purposes of managing the patient's treatment. In the past, some Medicare contractors have denied claims based on either ambiguous or missing information in the laboratory's report.

Conclusion

Entities affected by the Medicare NCD, including health systems, clinical laboratories, health care professionals, and patients, should carefully assess its impact on their current and future activities and the potential opportunities to influence CMS Medicare coverage going forward. Although national coverage determinations are usually CMS's final position on Medicare coverage, stakeholders may need to seek CMS guidance in specific cases. Moreover, significant issues may form the basis for a request to reopen the Medicare NCD so that it can be revised to reflect changes in technology, clinical evidence, and patient outcomes. Finally, since the Medicare NCD is limited to Medicare coverage, it remains to be seen how the Medicare program will determine reimbursement rates for NGS tests.

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